

CLAIMS

1. A method of isolating a quantity of cells, comprising the steps of:

(a) placing a sample including an amount of target cells and unwanted material into a cuvette;

(b) removing an amount of unwanted material from said sample in said cuvette;

(c) measuring at least one parameter of said sample remaining in said cuvette related to the number of target cells in said sample; and

(d) withdrawing a portion of said sample remaining in said cuvette when said parameter is within selected limits.

2. A method as claimed in claim 1, further comprising the steps of repeating steps (a) through (c) if said parameter indicates that a predetermined quantity of said target cells is not present in said sample remaining in said cuvette.

3. A method as claimed in claim 1, wherein said parameter of said sample includes the turbidity of said sample.

4. A method as claimed in claim 3, wherein said turbidity is estimated by administering an amount of light onto said sample and measuring the amount of light scattering, therein indicating the quantity of target cells per unit volume of measured sample volume.

5. A method as claimed in claim 1, further comprising the steps of adjusting the volume of said portion of said sample removed from said cuvette so that a predetermined quantity of said target cells are removed.

6. A method as claimed in claim 1, wherein said parameter of said sample is a measured amount of filter resistance.

7. A method as claimed in claim 1, wherein said step of withdrawing said portion of said sample remaining in said cuvette is initiated after a predetermined period of time after said step of placing said sample in said cuvette.

8. A method as claimed in claim 7, further comprising the step of measuring at least one second parameter related to the amount of said unwanted material in said sample and wherein said predetermined period of time is determined by said amount of said unwanted material in said sample.

9. A method as claimed in claim 7, further comprising the step of measuring at least one second parameter related to a quality of the amount of said unwanted material in said sample and wherein said predetermined period of time is determined by said quality of said unwanted material in said sample.

10. A method as claimed in claim 1, further comprising the step of mixing said sample in a sample container prior to said step of placing said sample into said cuvette.

11. A method as described in claim 10, wherein said sample container has a container liquid contained therein, whereby said sample and said container liquid form a suspension.

12. A method as described in claim 11, wherein said container liquid is a preservative.

13. A method as claimed in claim 1, wherein said portion of said sample withdrawn from said cuvette is selected so that an approximately known quantity of target cells are withdrawn.

14. A method as claimed in claim 1, wherein said sample is in the form of a suspension of cells in a fluid during said removing step.

15. A method as claimed in claim 14, further comprising the step of suspending said sample in a fluid to form said suspension.

16. A method as claimed in claim 14, wherein said step of suspending said sample in a fluid suspension is done prior to placing said sample into said cuvette.

17. A method as claimed in claim 14, wherein said fluid suspension is a liquid suspension.

18. A method as claimed in claim 17, wherein said portion of said sample withdrawn from said cuvette is fixed

and further comprising the step of adding or subtracting fluid from said suspension within said cuvette while substantially retaining target cells in said cuvette so that an approximately known quantity of target cells are withdrawn.

19. A method as claimed in claim 14, further comprising the step of adding at least one reagent to said fluid suspension, said reagent selected from the group consisting of: a lysing agent, an adhesion conditioning agent, a washing agent, a mucolytic agent, an amount of preservative solution, and water.

20. A method as claimed in claim 14, further comprising the step of transferring an amount of said portion of said sample removed from said cuvette to a slide.

21. A method as claimed in claim 20, wherein said slide further has a hydrophobic boundary surrounding said area, said hydrophobic boundary facilitating containment of said portion of said sample onto said slide.

22. A method as claimed in claim 20, further comprising the step of settling a portion of said sample onto said slide to form a monolayer of cells.

23. A method as claimed in claim 22, wherein said settling step occurs on said slide within an area defined by a containment area.

24. A method as claimed in claim 22, wherein an area on said slide has an adhesive thereon, said adhesive facilitating formation of said monolayer.

25. A method as claimed in claim 22, further comprising the step of removing excess fluid of said sample from said slide after said settling step.

26. A method as claimed in claim 24, wherein said adhesive is a ultraviolet light polymerizable adhesive, the method further comprising applying ultraviolet light to said adhesive during or after said settling step.

27. A method as claimed in claim 24, wherein said adhesive is a polycationically charged polymer.

28. A method as described in claim 25, wherein said step of removing a portion of excess fluid of said sample from said slide comprises aspirating said excess fluid of said sample from said slide after said monolayer of said target cells have formed on said slide.

29. A method as described in claim 25, wherein said step of removing a portion of said excess fluid of said sample from said slide comprises draining said slide by tilting said slide after said monolayer of said target cells have formed on said slide.

30. A method as described in claim 25, wherein said step of removing a portion of said excess fluid of said sample from said slide comprises absorbing said excess from said slide after said monolayer of said target cells have formed on said slide.

31. A method as described in claim 25, further comprising the step of fixing said target cells by applying alcohol solution to said monolayer.

32. A method as claimed in claim 2, wherein said removing step comprises filtering said sample in said cuvette such that said fluid and unwanted material passes in a downstream direction through a filter connected to said cuvette having an upstream side facing the interior of said cuvette and a downstream side, said target cells being substantially retained within said cuvette on or above said upstream side of said filter.

33. A method as claimed in claim 32, wherein said suspension includes a preservative solution and said preservative solution is removed from said cuvette in said filtering step, the method further comprises replacing said preservative solution with a clean resuspension liquid prior to said step of withdrawing a portion of said sample remaining in said cuvette.

34. A method as claimed in claim 32, wherein said filtering is discontinued when a predetermined level of said sample remaining in said cuvette is obtained.

35. A method as claimed in claim 32, wherein said method further comprises the step of monitoring a pressure differential between said upstream side and said downstream side and discontinuing filtering when a predetermined level of said differential pressure is obtained.

36. A method as claimed in claim 32, wherein said step of filtering said sample remaining in said cuvette comprises applying a subatmospheric pressure on the downstream side of said filter to pull said unwanted sample material through said filter.

37. A method as claimed in claim 32, further comprising the step of passing a fluid through said filter into said cuvette in an upstream direction from said downstream side of said filter to said upstream side of said filter so as to facilitate said filtering step and further mix said sample within said cuvette.

38. A method as claimed in claim 37, wherein said step of passing fluid through said filter in said upstream direction is performed concurrently with said step of measuring a parameter of said sample remaining in said cuvette.

39. A method as claimed in claim 37, wherein said fluid is water.

40. A method as claimed in claim 37, wherein said fluid is a gas.

41. A method as claimed in claim 37, wherein said fluid is air.

42. A method as claimed in claim 37, wherein said fluid is a mixture of a liquid and gas.

43. A method as claimed in claim 37, wherein said fluid passing in said upstream direction through said filter includes filtrate which had previously passed downstream through said filter.

44. A method as claimed in claim 37, wherein said filtering step and said step of passing a fluid through said

filter in said upstream direction are conducted so that fluid flows alternately in said downstream and upstream directions.

45. A method as claimed in claim 44, wherein said fluid flow alternates between upstream and downstream directions at a frequency of about .01 to about 50 Hz.

46. A method as claimed in claim 45, wherein said frequency is about 5 to about 15 Hz when said fluid is a liquid and is about 0.2 to 1 Hz when said fluid is a gas.

47. A method as claimed in claim 1, wherein said measuring step comprises administering an amount of electromagnetic interrogation to said sample in said cuvette and measuring a response to said interrogation, said response being associated with a property of said target cells or said unwanted material in said sample.

48. A method as claimed in claim 1, wherein said step of placing said sample into said cuvette is accomplished by a pipette.

49. A method as claimed in claim 48, wherein said step of placing said sample into said cuvette by said pipette mixes the portion of said sample in said cuvette.

50. A method of preparing a monolayer of cells, comprising the steps of:

(a) suspending a sample in a fluid, said sample including an amount of target cells and unwanted material;

(b) placing a portion of said suspended sample into a cuvette;

(c) removing an amount of said unwanted material from said suspended sample in said cuvette;

(d) measuring at least one parameter of said sample remaining in said cuvette related to the number of said target cells in said sample;

(e) repeating steps (b) through (d) if said parameter indicates that a predetermined quantity of said target cells is not present in said sample remaining in said cuvette;

(f) withdrawing a portion of said sample remaining in said cuvette when said parameter is within selected limits; and

(g) transferring said withdrawn portion to a slide.

51. A method as claimed in claim 50, further comprising the step of resuspending said sample in a fluid after said removing step and prior to said step of measuring at least one parameter of said sample remaining in said cuvette.

52. A method of automatically preparing series of monolayers of cells from a series of samples, comprising the steps of:

(a) suspending each sample in a fluid, said sample including an amount of target cells and unwanted material;

(b) placing a portion of each said suspended sample into a cuvette;

(c) removing an amount of said unwanted material from each said suspended sample in said cuvette;

(d) for at least some of said samples, measuring at least one parameter of the sample remaining in the cuvette containing that sample, said parameter being related to the number of said target cells in that sample remaining in the cuvette;

(e) for at least some samples subjected to step (d), repeating steps (b) through (d) for a particular sample if said parameter for that sample indicates that a predetermined quantity of said target cells is not present in that sample remaining in said cuvette;

(f) for at least some of those samples subjected to step (d) withdrawing a portion of said sample remaining in said cuvette when said parameter is within selected limits; and

(g) transferring at least a part of each said withdrawn portion to a slide.

53. A method as claimed in claim 52, wherein said parameter of said sample includes the turbidity of said sample.

54. A method as claimed in claim 52, further comprising the step of resuspending said sample in a fluid after said removing step and prior to said step of measuring at least one parameter of said sample remaining in said cuvette.

55. A method as claimed in claim 53, wherein said turbidity is estimated by administering an amount of light onto said sample and measuring the amount of light scattering, therein indicating the quantity of said target cells per unit volume of measured sample volume.

56. A method as claimed in claim 52, further comprising the step of determining whether said removing step has been completed within a predetermined time, and subjecting to step (d) only those samples for which said removing step is completed within a predetermined time, the method further comprising withdrawing a portion of each sample which is not subjected to step (d) and transferring the withdrawn portion to a slide.

57. A method as claimed in claim 56, wherein said removing step includes filtering substantially all fluid from the sample.

58. A method as claimed in claim 57, further comprising the step of resuspending said sample in a fluid after said removing step and prior to said step of measuring at least one parameter of said sample remaining in said cuvette.

59. A method as claimed in claim 52, wherein all of said samples are subjected to step (d).

60. A method of preparing a monolayer of cells, comprising the steps of:

(a) suspending a sample in a fluid, said sample including an amount of target cells and unwanted material;

(b) placing a portion of said suspended sample into a cuvette;

(c) removing an amount of unwanted material from said suspended sample in said cuvette;

(d) measuring the length of time from a period starting at the initiation of said step of removing an amount of unwanted material from said suspended sample in said cuvette;

(e) withdrawing a portion of said sample remaining in said cuvette when said period of time reaches a predetermined period; and

(f) transferring said withdrawn portion to a slide.

61. A method as claimed in claim 60, further comprising the step of measuring at least one parameter of said sample related to the number of said target cells in said sample, and wherein said predetermined period is related to said number of said target cells in said sample.

62. A method as claimed in claim 60, further comprising the step of measuring at least one parameter of said sample related to a quality of said unwanted material in said sample, and wherein said predetermined period is related to said quality of said unwanted material in said sample.

63. A method as claimed in claim 60, further comprising the step of measuring at least one parameter of said sample related to a quantity of said unwanted material in said sample, and wherein said predetermined period is related to said quantity of said unwanted material in said sample.

64. A method as claimed in claim 60, further comprising the step of resuspending said sample in a fluid after said removing step and prior to said step of withdrawing a portion of said sample remaining in said cuvette.

65. A method of preparing a monolayer of cells, comprising the steps of:

(a) suspending a sample in a fluid, said sample including an amount of target cells and unwanted material;

(b) placing a portion of said suspended sample into a cuvette;

(c) removing an amount of unwanted material from said suspended sample in said cuvette;

(d) measuring at least one parameter of said sample related to the number of said target cells in said sample;

(e) measuring the length of time from a period starting at the initiation of said step of removing an amount of unwanted material from said suspended sample in said cuvette;

(f) repeating steps (b) through (d) if said parameter indicates that a predetermined quantity of said target cells is not present in said sample remaining in said cuvette; and

(g) transferring said withdrawn portion to a slide.

66. A method as claimed in claim 65, further comprising the step of withdrawing a portion of said sample remaining in said cuvette when said period of time reaches a predetermined period.

67. A method as claimed in claim 65, further comprising the step of withdrawing a portion of said sample remaining in said cuvette when a predetermined number of repetitions of said steps (b) through (d) have been completed.

68. A method of collecting cells, comprising the steps of:

(a) providing a suspension including cells and a liquid in a container having an interior, an aperture in communication with said interior, and a filter sized so that said cells cannot pass through such filter, said filter having an upstream side facing the interior of said container and a downstream side;

(b) causing fluid to flow fluid through said filter in an alternating manner in a downstream direction from said upstream side of said filter to said downstream side of said filter and in an upstream direction opposite to said downstream direction.

69. A method of collecting cells, comprising the steps of:

(a) introducing a quantity of cells and a fluid into a container having an interior, an aperture in communication with said interior, and a filter covering said aperture so that at least a portion of said cells cannot pass through said filter,

(b) filtering said fluid through said filter, thereby collecting said portion of said cells in said container, at least a portion of said fluid being withdrawn and reintroduced into said container proximate enough to said filter to reduce blockage of said filter.

70. A method as claimed in claim 69, wherein at least a part of said step of introducing said fluid is performed contemporaneously with said step of filtering said liquid.

71. A method as claimed in claim 69, wherein said quantity of cells is suspended in said fluid prior to said step of introducing said quantity of cells and said fluid into said container.

72. A method of collecting cells, comprising the steps of:

(a) providing a quantity of cells and a fluid in a container having an upstream interior section, a downstream interior section and a choke having a lesser cross-sectional area than said upstream and downstream sections, said upstream and downstream sections communicating with one another through said choke, said container also having a filter remote from said choke in communication with said downstream interior section, said filter being sized so that at least a portion of said cells cannot pass through said filter; and

(b) drawing said fluid from said upstream interior section through said choke, said downstream interior section and said filter, such that fluid passing through said choke facilitates mixing of said fluid and said cells in said downstream section.

73. An apparatus for holding and mixing specimens, comprising:

(a) a container having at least one wall defining an interior space and an opening;

(b) at least one projection projecting from said wall into said interior space, said projection adapted to facilitate transfer of specimens into said interior of said

container and facilitate mixing of specimens placed into said interior of said container.

74. The apparatus as claimed in claim 73, wherein said projection is adapted to facilitate transfer of specimens from a spatula.

75. The apparatus as claimed in claim 73, wherein said projection is adapted to facilitate transfer of specimens from a brush.

76. The apparatus as claimed in claim 73, further comprising a cap releasably attached to said container for closing said opening.

77. The apparatus as claimed in claim 73, wherein said projection includes at least two fingers extending from said wall into said interior space.

78. The apparatus as claimed in claim 77, wherein said at least two fingers are spaced apart from one another by about 1 to about 6 mm.

79. An apparatus for collecting cells from a fluid, comprising:

(a) a container having an upstream interior section, a downstream interior section, and a choke having a lesser cross-sectional area than said upstream and downstream sections, said upstream and downstream sections communicating with one another through said choke; and

(b) a filter remote from said choke in communication with said downstream interior section, said filter being sized so that at least a portion of said cells cannot pass through said filter, whereby when a fluid is drawn from said upstream interior section through said choke, said downstream interior section, and said filter, movement of fluid passing through said choke facilitates mixing of said fluid and said cells in said downstream section.

80. An apparatus as claimed in claim 79, further comprising:

a pipette for introducing said fluid into said container, said pipette having a first end adapted to pass through said

intermediate interior section of said container so that fluid can be introduced into said container in said second interior section.

81. An apparatus as claimed in claim 79, further comprising:

a pipette for withdrawing said fluid from said container, said pipette having a first end adapted to pass through said intermediate interior section of said container so that fluid can be withdrawn from said second interior section of said container.

82. An apparatus as claimed in claim 80, wherein at least one of said pipette and said container has a stop operable to prevent said first end of said pipette from coming into contact with said filter.

83. An apparatus as claimed in claim 80, wherein at least one of said pipette and said container has a stop operable to direct said first end of said pipette to a point proximate to said filter.

84. Apparatus for filtering cells from a liquid comprising:

(a) an container having an interior space, an opening at an upstream end of said interior space, and a filter adapted to retain cells, said filter communicating with said interior space downstream of said opening; and

(b) a pipette having a discharge opening, said pipette being constructed and arranged so that said pipette can be positioned within said interior space, at least one of said pipette and said container has a stop operable to arrest motion of said pipette into said opening so that said discharge opening of said pipette is disposed proximate to said filter when said stop arrests said motion.

85. An apparatus as claimed in claim 84, wherein said pipette is disposed about 0.1 mm to about 1 mm to said filter.

86. A slide assembly for microscopic examination of cells, comprising:

(a) a slide having a surface;

(b) an adhesive coating on at least a portion of said surface; and

(c) a ring surrounding a portion of said adhesive coating, said ring having a lower surface energy than said adhesive portion.

87. A slide as claimed in claim 86, wherein said ring is substantially transparent to the light used for microscopic examination.

88. A slide as claimed in claim 86, wherein said ring is substantially transparent to visible light.